

Table 1. Demographic characteristics of the study population	
Age (years)	Mean (SD)
18-24	20.5 (2.5)
25-34	29.5 (4.5)
35-44	39.5 (5.5)
45-54	49.5 (6.5)
55-64	59.5 (7.5)
65-74	69.5 (8.5)
75-84	79.5 (9.5)
85-94	89.5 (10.5)
95-104	99.5 (11.5)
105-114	109.5 (12.5)
115-124	119.5 (13.5)
125-134	129.5 (14.5)
135-144	139.5 (15.5)
145-154	149.5 (16.5)
155-164	159.5 (17.5)
165-174	169.5 (18.5)
175-184	179.5 (19.5)
185-194	189.5 (20.5)
195-204	199.5 (21.5)
205-214	209.5 (22.5)
215-224	219.5 (23.5)
225-234	229.5 (24.5)
235-244	239.5 (25.5)
245-254	249.5 (26.5)
255-264	259.5 (27.5)
265-274	269.5 (28.5)
275-284	279.5 (29.5)
285-294	289.5 (30.5)
295-304	299.5 (31.5)
305-314	309.5 (32.5)
315-324	319.5 (33.5)
325-334	329.5 (34.5)
335-344	339.5 (35.5)
345-354	349.5 (36.5)
355-364	359.5 (37.5)
365-374	369.5 (38.5)
375-384	379.5 (39.5)
385-394	389.5 (40.5)
395-404	399.5 (41.5)
405-414	409.5 (42.5)
415-424	419.5 (43.5)
425-434	429.5 (44.5)
435-444	439.5 (45.5)
445-454	449.5 (46.5)
455-464	459.5 (47.5)
465-474	469.5 (48.5)
475-484	479.5 (49.5)
485-494	489.5 (50.5)
495-504	499.5 (51.5)
505-514	509.5 (52.5)
515-524	519.5 (53.5)
525-534	529.5 (54.5)
535-544	539.5 (55.5)
545-554	549.5 (56.5)
555-564	559.5 (57.5)
565-574	569.5 (58.5)
575-584	579.5 (59.5)
585-594	589.5 (60.5)
595-604	599.5 (61.5)
605-614	609.5 (62.5)
615-624	619.5 (63.5)
625-634	629.5 (64.5)
635-644	639.5 (65.5)
645-654	649.5 (66.5)
655-664	659.5 (67.5)
665-674	669.5 (68.5)
675-684	679.5 (69.5)
685-694	689.5 (70.5)
695-704	699.5 (71.5)
705-714	709.5 (72.5)
715-724	719.5 (73.5)
725-734	729.5 (74.5)
735-744	739.5 (75.5)
745-754	749.5 (76.5)
755-764	759.5 (77.5)
765-774	769.5 (78.5)
775-784	779.5 (79.5)
785-794	789.5 (80.5)
795-804	799.5 (81.5)
805-814	809.5 (82.5)
815-824	819.5 (83.5)
825-834	829.5 (84.5)
835-844	839.5 (85.5)
845-854	849.5 (86.5)
855-864	859.5 (87.5)
865-874	869.5 (88.5)
875-884	879.5 (89.5)
885-894	889.5 (90.5)
895-904	899.5 (91.5)
905-914	909.5 (92.5)
915-924	919.5 (93.5)
925-934	929.5 (94.5)
935-944	939.5 (95.5)
945-954	949.5 (96.5)
955-964	959.5 (97.5)
965-974	969.5 (98.5)
975-984	979.5 (99.5)
985-994	989.5 (100.5)
995-1004	999.5 (101.5)
1005-1014	1009.5 (102.5)
1015-1024	1019.5 (103.5)
1025-1034	1029.5 (104.5)
1035-1044	1039.5 (105.5)
1045-1054	1049.5 (106.5)
1055-1064	1059.5 (107.5)
1065-1074	1069.5 (108.5)
1075-1084	1079.5 (109.5)
1085-1094	1089.5 (110.5)
1095-1104	1099.5 (111.5)
1105-1114	1109.5 (112.5)
1115-1124	1119.5 (113.5)
1125-1134	

In re Application of:

Continuation of

Group Art Unit: 0000

Examiner: Unknown

PRELIMINARY AMENDMENT

Sir:

IN THE SPECIFICATION:

Please amend the specification as follows:

Page 1, before line 5, insert

-- This Application is a Continuation of PCT/GB99/03728 filed November 9, 1999, which claims benefit of priority under 35 U.S.C. § 365(c) and § 120; which claims benefit under 35 U.S.C. § 119(e) of U.S. Provisional Application No. 60/107,655, filed November 9, 1998. The disclosure of PCT/GB99/03728 is incorporated herein by reference. --.

PRELIMINARY AMENDMENT
Cont. of PCT/GB99/03728

IN THE CLAIMS:

Please amend the claims as follows:

Claim 3. (Amended) A method as claimed in claim 1, wherein said antibacterial agent is used at a concentration of 25 to 150 μ g/ml with bacteria present at a concentration of 10^5 to 10^9 bacteria/ml.

Claim 4. (Amended) A method as claimed in claim 1, wherein said bacteria are *Staphylococcus aureus*, *Escherichia coli*, *Haemophilus influenzae*, *Streptococcus pyogenes*, *Streptococcus gordonii* or *Mycobacterium tuberculosis*.

Claim 5. (Amended) A method as claimed in claim 1, wherein said bacteria are *Mycobacterium tuberculosis* and said antibacterial agent is rifampicin.

Claim 6. (Amended) A method as claimed in claim 1, wherein said bacteria are *Escherichia coli* and said antibacterial agent is kanamycin.

Claim 7. (Amended) A method as claimed in claim 1, wherein said bacteria are *Staphylococcus aureus* and said antibacterial agent is ampicillin.

Claim 8. (Amended) A phenotypically antibiotic-resistant subpopulation of stationary phase bacteria, obtainable by a method as defined in claim 1.

Claim 9. (Amended) A process for assessing the antibacterial activity of a test compound or agent or for isolating a compound or agent having antibacterial activity against stationary phase bacteria comprising the steps of:

PRELIMINARY AMENDMENT
Cont. of PCT/GB99/03728

(i) preparing a phenotypically antibiotic-resistant subpopulation of stationary phase bacteria according to the method defined in claim 1;

(ii) incubating a sample of said phenotypically resistant subpopulation with one or more test compounds or agents; and

(iii) assessing any antibacterial effects against said phenotypically resistant subpopulation and optionally isolating a compound or agent exhibiting antibacterial activity.

Claim 11. (Amended) An antibacterial agent identified or prepared according to the process defined in claim 10.

Claim 13. (Amended) A composition comprising an antibacterial agent or chemical compound as defined in claim 12 and a pharmaceutically acceptable excipient or diluent.

Claim 14. (Amended) A formulation comprising at least one antibacterial agent having activity against actively growing bacteria and at least one antibacterial agent or chemical compound having activity against a phenotypically antibiotic-resistant subpopulation of stationary phase bacteria as defined in claim 13, wherein said formulation is presented as a combined preparation for simultaneous, separate or sequential use in the treatment of a bacterial infection.

Claim 15. (Amended) An antibacterial agent or chemical compound as defined in claim 13 for use in the treatment of a bacterial infection.

Claim 16. (Amended) Use of an antibacterial agent or chemical compound as defined in claim 13 in the preparation of a medicament for the treatment of a bacterial infection.

PRELIMINARY AMENDMENT
Cont. of PCT/GB99/03728

Claim 17. (Amended) A method of treating of a bacterial infection comprising administering to a patient in need of such therapy an effective amount of an antibacterial agent or chemical compound as defined in claim 13.

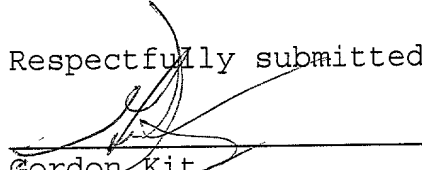
Claim 19. (Amended) A formulation, agent, compound, use of method as claimed in claim 14, where said bacterial infection is characterized by a subpopulation of persistent bacteria which may enter a dormant phase after infection.

REMARKS

The specification has been amended to insert formal matter and the claims have amended to delete their multiply dependency in order to make the application consistent with U.S. patent practice. Hence, the amendment of the specification and claims does not constitute new matter.

The Examiner is invited to contact the undersigned at his Washington telephone number on any questions which might arise.

Respectfully submitted,


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Date: April 27, 2001

A P P E N D I X

Marked-up Version of Amended Application

The Specification is amended as follows:

Page 1, before line 5, insert

-- This Application is a Continuation of PCT/GB99/03728 filed November 9, 1999, which claims benefit of priority under 35 U.S.C. § 365(c) and § 120; which claims benefit under 35 U.S.C. § 119(e) of U.S. Provisional Application No. 60/107,655, filed November 9, 1998. The disclosure of PCT/GB99/03728 is incorporated herein by reference. --.

The Claims are amended as follows:

Claim 3. (Amended) A method as claimed in claim 1, [or 2] wherein said antibacterial agent is used at a concentration of 25 to 150 µg/ml with bacteria present at a concentration of 10⁵ to 10⁹ bacteria/ml.

Claim 4. (Amended) A method as claimed in [any one of claims 1 to 3] claim 1, wherein said bacteria are *Staphylococcus aureus*, *Escherichia coli*, *Haemophilus influenzae*, *Streptococcus pyogenes*, *Streptococcus gordonii* or *Mycobacterium tuberculosis*.

Claim 5. (Amended) A method as claimed in [any one of claims 1 to 4] claim 1, wherein said bacteria are *Mycobacterium tuberculosis* and said antibacterial agent is rifampicin.

Claim 6. (Amended) A method as claimed in [any one of claims 1 to 4] claim 1, wherein said bacteria are *Escherichia coli* and said antibacterial agent is kanamycin.

Claim 7. (Amended) A method as claimed in [any one of claims 1 to 4] claim 1, wherein said bacteria are

Staphylococcus aureus and said antibacterial agent is ampicillin.

Claim 8. (Amended) A phenotypically antibiotic-resistant subpopulation of stationary phase bacteria, obtainable by a method as defined in [any one of claims 1 to 7] claim 1.

Claim 9. (Amended) A process for assessing the antibacterial activity of a test compound or agent or for isolating a compound or agent having antibacterial activity against stationary phase bacteria comprising the steps of:

(i) preparing a phenotypically antibiotic-resistant subpopulation of stationary phase bacteria according to the method defined in [an one of claims 1 to 7] claim 1;

(ii) incubating a sample of said phenotypically resistant subpopulation with one or more test compounds or agents; and

(iii) assessing any antibacterial effects against said phenotypically resistant subpopulation and optionally isolating a compound or agent exhibiting antibacterial activity.

Claim 11. (Amended) An antibacterial agent identified or prepared according to the process defined in claim [9 or] 10.

Claim 13. (Amended) A composition comprising an antibacterial agent or chemical compound as defined in claim [11 or] 12 and a pharmaceutically acceptable excipient or diluent.

Claim 14. (Amended) A formulation comprising at least one antibacterial agent having activity against actively growing bacteria and at least one antibacterial agent or chemical compound having activity against a phenotypically antibiotic-resistant subpopulation of stationary phase bacteria as defined in claim [12 or] 13, wherein said formulation is presented as a combined preparation for simultaneous, separate or sequential use in the treatment of a bacterial infection.

Claim 15. (Amended) An antibacterial agent or chemical compound as defined in claim [12 or] 13 for use in the treatment of a bacterial infection.

Claim 16. (Amended) Use of an antibacterial agent or chemical compound as defined in claim [12 or] 13 in the preparation of a medicament for the treatment of a bacterial infection.

Claim 17. (Amended) A method of treating of a bacterial infection comprising administering to a patient in need of such therapy an effective amount of an antibacterial agent or chemical compound as defined in claim [12 or] 13.

Claim 19. (Amended) A formulation, agent, compound, use of method as claimed in [any one of] claim 14 [to 18], where said bacterial infection is characterized by a subpopulation of persistent bacteria which may enter a dormant phase after infection.